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EXAMINER	
LAM, ANN Y	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 12/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/960,716	TCHAGA, GRIGORIY S.	
	Examiner	Art Unit	
	Ann Y. Lam	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 29, 2006 has been entered.

Status of Claims

Claims 2 and 20-45 are canceled.

Claims 1 and 3-19 are pending.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1, 3-5, 12, 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Margherita, 4,111,656, in view of Zarling et al., 5,674,698, and further

in view of Kartel et al., "Evaluation of Pectin Binding of Heavy Metal Ions in Aqueous Solutions", Chemosphere, Vol. 38, No. 11, pp. 2591-2596, 1999.

Margherita teaches the invention substantially as claimed. More specifically, as to claims 1 and 3 through 5, Margherita teaches a method of determining whether a sample includes an analyte of interest, said method comprising:

pre-incubating said sample with a first buffer composition comprising a metal ion chelating polysaccharide(see col. 5, lines 9-21, disclosing a chelating agent such as ethylene tetraacetic acid, i.e., EDTA, for chelating unwanted metal ions),

contacting said sample with a plurality of distinct binding agents (see col. 5, lines 47-51),

wherein each of said binding agents at least comprises a specific epitope binding domain of an antibody (see col. 5, line 50);

detecting the presence of any resultant binding complexes on said surface to obtain analyte binding data (see col. 5, lines 54-56);

and employing said analyte binding data to determine whether said sample includes said at least one analyte of interest (see col. 5, lines 57-58).

However, Margherita does not teach that the antibody is bound to a solid support in an array.

Zarling et al. however teach that heterogeneous assays are usually preferred and are generally more sensitive and reliable than homogenous assay (col. 20, lines 33-35). Zarling et al. also give an example of a radioimmunoassay (col. 20, lines 25-26). Also, as an example, Zarling et al. disclose a solid substrate having a plurality of distinct

species of first binding component in an array of peptides and then contacting the solid support with an analyte solution and detecting subsequent binding (col. 23, line 62 – col. 24, line 5).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the Margherita assay, which is disclosed as a homogenous assay, such that the antibodies are immobilized on a solid phase in a heterogenous assay as taught by Zarling et al. because Zarling et al. teach that heterogeneous assays are preferred because they are more sensitive and reliable than homogenous assays. Given the disclosure by Zarling et al. of a heterogeneous radioimmunoassay, one of ordinary skill in the art would have reasonable expectation of success in modifying the Margherita assay into a heterogeneous assay as taught by Zarling et al.

Zarling et al. also teach, as to dependent claim 12, a plurality of washings steps between said contacting and detecting steps by teaching that bound complexes are typically isolated from unbound material prior to detection and usually by incorporating at least one washing stop to removed background signal attributable to label present in unbound material (col. 20, lines 61-64), and giving an example of washing twice (col. 51, lines 59-60).

Also, as to independent claim 1, although Margherita teaches that the buffer solution contains a chelating agent for chelating unwanted metal ions and discloses ethylenediamine tetraacetic acid, i.e., EDTA, as an example (col. 5, lines 17-21), Margherita does not teach that the metal chelating agent may be a polysaccharide,

such as apple pectin (as claimed in claims 1, 3-5 and 14-16). However, Kartel et al. teach the motivation to use a polysaccharide, such as apple pectin.

Kartel et al. teach that polysaccharides such as apple pectin is a metal chelator that has a high selectivity for certain metals (see page 2591-2592 and page 2595).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize apple pectin as the metal ion chelator generally disclosed by Kartel et al. as the specific metal ion chelator generally disclosed by Margherita because Kartel et al. teach that apple pectin provides the advantage of having high selectivity towards metal ions and is efficient in absorbing metal ions. That is, while Margherita teaches the general use of a chelating agent (and discloses EDTA only as an example), Kartel et al. teach that the motivation for using apple pectin as the metal chelator by teaching that apple pectin is a metal chelator that has high affinity towards certain metal ions (see bottom of page 2595 for example). While the Kartel et al. reference does not disclose use of apple pectin in an assay other than the assay for the evaluation of the binding affinity of apple pectin, the reference nevertheless discloses that apple pectin acts as a metal ion chelator in an *in vitro assay*, and the Kartel et al. reference is analogous art because it relates to the same problem to be solved in the Margherita reference, i.e., metal chelating. Moreover, one of ordinary skill in the art would have reasonable expectation of success in utilizing apple pectin as the specific chelating agent generically disclosed by Margherita because Margherita do not limit the disclosed assay to any particular metal chelator but rather teach the use of a metal

chelator in general (col. 13, lines 57-58), and also because Kartel et al. teach that the apple pectin shows this high affinity for certain metal ions in an *in vitro* assay.

As to claim 18, Margherita discloses that the method further comprises a sample fractionating step prior to said contacting step (see col. 12, lines 3-11, disclosing extraction in a chromatographic column in a buffer).

As to claim 19, Margherita discloses that the fractionating step comprises contacting said sample with at least one affinity column (see col. 12, lines 3-11).

2. Claims 6-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Margherita, 4,111,656, in view of Zarling et al., 5,674,698, and further in view of Kartel et al., "Evaluation of Pectin Binding of Heavy Metal Ions in Aqueous Solutions", Chemosphere, Vol. 38, No. 11, pp. 2591-2596, 1999, Schoemaker et al., 4,837,167, and Pronovost et al., 5,773,234.

Margherita in view of Zarling et al. and Kartel et al. disclose the invention substantially as claimed (see above with respect to claim 1). While Margherita does teach that the assay method may include extracting the analyte using a buffer (see col. 12, line 10). While Margherita discloses extracting an analyte from a cellular source (see for example, col. 12, line 3), Margherita does not disclose labeling the extracted analyte, wherein said extracting and labeling steps employ the same buffer composition.

However, Schoemaker et al. teach that labeling an analyte prior to the step of contacting the analyte to the immobilized probed provides the advantage of eliminating a washing step and an improvement in kinetics of the reaction (see col. 2, lines 15-35).

It would have been obvious to one of ordinary skill at the time the invention was made to label the analyte in the invention taught by Margherita in view of Zarling et al. and Kartel et al. as taught by Schoemaker et al. because Schoemaker et al. teach that this provides the advantages of eliminating a washing step and improving reaction kinetics.

Also, as to the limitation regarding employing the same buffer composition for the extraction and labeling step, Pronovost et al. teach this limitation.

Pronovost et al. teach using a buffer in an extraction step, the buffer increasing the sensitivity of the assay, and preferably using the same buffer composition during labeling (col. 4, lines 48-61). It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the same buffer composition in the invention taught by Margherita in view of Zarling et al. and Kartel et al. because Pronovost et al. teach that using the same buffer, which increases sensitivity of the assay, in the labeling step is preferable. Given the teachings of Pronovost et al. of using the same buffer composition for the extraction step as the labeling step, one of ordinary skill in the art would have reasonable expectation of success in utilizing the same buffer for the extraction and labeling step in the invention taught by Margherita in view of Zarling et al. and Kartel et al.

As to the following claims, Margherita teaches the following regarding the buffer.

As to claim 7, said buffer composition is free of components that include primary amine moieties (col. 5, lines 17-22.)

As to claim 8, said buffer composition has a pH ranging from about 7 to about 12 (col. 5, lines 21-22.)

As to claim 9, while Margherita teaches that the buffer containing metal chelating polysaccharide is used in the assay (col. 12, lines 26-37), and Margherita also teaches extracting proteins from a cellular source using a buffer in a chromatographic column (see col. 12, lines 1-12), Margherita does not specify what comprises the extraction buffer nor that that the buffer composition is capable of extracting at least about 95% of the proteins of an initial cellular source. However, Pronovost et al. teach using the same buffer, which increases sensitivity of the assay, in the labeling step and capturing step is preferable. Given the teachings of Pronovost et al. of using the same buffer composition for the extraction step as the labeling step and capturing step (see col. 4, lines 58-61), one of ordinary skill in the art would have reasonable expectation of success in utilizing the same buffer for the assay or capturing step as for the extraction step. As to extracting at least 95% of the proteins form the cellular source, while Margherita does not disclose this, Marherita does disclose an extraction step using a chromatographic column (see col. 12, lines 1-12). Also, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. In re Aller, 1-5 USPQ 233. In this case, Margherita in view of Zarling et al., Kartel et al., Schoemaker et al. and Pronovost et al. discloses the general conditions of the claim and extracting at least 95% of the proteins from the cellular source is an optimum or workable range (e.g., utilizing the chromatographic column and buffer) and thus involves only routine skill in the art.

3. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Margherita, 4,111,656, in view of Zarling et al., 5,674,698, and further in view of Kartel et al., "Evaluation of Pectin Binding of Heavy Metal Ions in Aqueous Solutions", Chemosphere, Vol. 38, No. 11, pp. 2591-2596, 1999, and Wohlstadter et al., 6,207,369.

Margherita in view of Zarling et al. and Kartel et al. teach the invention substantially as claimed (see above with respect to claim 1), except for determining the presence of at least two distinct analytes in said sample.

However, Wohlstadter et al teach that an array of immobilized probes may have different geometric shapes representing binding domains specific for different analytes (col. 8, lines 20-23). It would have been obvious to one of ordinary skill in the art at the time the invention was made to provide different probes in the array in the invention taught by Margherita in view of Zarling et al. and Kartel et al. because Wohlstadter et al. teach that such an array of probes bind to different analytes. One of ordinary skill in the art would recognize that the array provides the benefit of detecting more than one analyte.

4. Claims 13-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Margherita, 4,111,656, in view of Zarling et al., 5,674,698, and further in view of Kartel et al., "Evaluation of Pectin Binding of Heavy Metal Ions in Aqueous Solutions", Chemosphere, Vol. 38, No. 11, pp. 2591-2596, 1999, Schoemaker et al., 4,837,167, and Pronovost et al., 5,773,234, and Wohlstadter et al., 6,207,369.

As to claims 13-16, Margherita in view of Zarling et al. and Kartel teach the invention substantially as claimed (see above with respect to claim 1).

While Margherita does teach that the assay method may include extracting the analyte from a cellular source using a buffer (see col. 12, lines 3-10), Margherita does not disclose labeling the extracted analyte, wherein said extracting and labeling steps employ the same buffer composition.

However, Schoemaker et al. teach that labeling an analyte prior to the step of contacting the analyte to the immobilized probed provides the advantage of eliminating a washing step and an improvement in kinetics of the reaction (see col. 2, lines 15-35). It would have been obvious to one of ordinary skill at the time the invention was made to label the analyte in the invention taught by Margherita in view of Zarling et al. and Kartel et al. as taught by Schoemaker et al. because Schoemaker et al. teach that this provides the advantages of eliminating a washing step and improving reaction kinetics.

Also, Margherita and Zarlng et al. and Kartel et al. do not teach employing the same buffer composition for the extraction and labeling step. However Pronovost et al. teach this limitation.

Pronovost et al. teach using a buffer in an extraction step, the buffer increasing the sensitivity of the assay, and preferably using the same buffer composition during labeling (col. 4, lines 48-61). It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the same buffer composition in the invention taught by Margherita in view of Zarling et al. and Kartel et al. because Pronovost et al. teach that using the same buffer, which increases sensitivity of the

assay, in the labeling step is preferable. Given the teachings of Pronovost et al. of using the same buffer composition for the extraction step as the labeling step, one of ordinary skill in the art would have reasonable expectation of success in utilizing the same buffer for the extraction and labeling step in the invention taught by Margherita in view of Zarling et al. and Kartel et al.

Also, Margherita does not teach determining the presence of at least two distinct analytes in said sample.

However, Wohlstadter et al. teach that an array of immobilized probes may have different geometric shapes representing binding domains specific for different analytes (col. 8, lines 20-23). It would have been obvious to one of ordinary skill in the art at the time the invention was made to provide different probes in the array in the invention taught by Margherita (in view of Zarling et al., Kartel et al., Schoemaker et al., and Pronovost et al.) because Wohlstadter et al. teach that such an array of probes bind to different analytes. One of ordinary skill in the art would recognize that the array provides the benefit of detecting more than one analyte.

5. Claims 1, 3-5, 10 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Velander et al., 5,328,603, in view of Zarling et al., 5,674,698, and further in view of Kartel et al., "Evaluation of Pectin Binding of Heavy Metal Ions in Aqueous Solutions", Chemosphere, Vol. 38, No. 11, pp. 2591-2596, 1999.

Velander et al. teach the invention substantially as claimed. More specifically, as to claims 1, 3-5 and 13-16, Velander et al. teach a method of determining whether a sample includes an analyte of interest, said method comprising:

Pre-incubating said sample with a first buffer composition comprising a metal ion chelating agent (see col. 13, lines 56-59, disclosing use of a chelating agent such as EDTA because 7D7 only binds protein C and prothrombin in the absence of metal ions),

contacting said sample with a plurality of distinct binding agents (antibody 7D7, see col. 13, line 39),

wherein each of said binding agents at least comprises a specific epitope binding domain of an antibody (col. 13, line 39);

detecting the presence of any resultant binding complexes on said surface to obtain analyte binding data (col. 14, lines 3-16);

and employing said analyte binding data to determine whether said sample includes said at least one analyte of interest (col. 14, lines 3-16).

While Velander et al. teach that the protein 7D7 is bound to a bead as the solid support, Velander et al. however do not teach that the protein may be bound to a solid support in an array.

Zarling et al. however teach that solid supports may be in the form of beads (see for example col. 23, line 57-58) or a solid substrate having a plurality of distinct species of first binding component in an array of peptides (col. 23, line 62 – col. 24, line 5). Zarling et al. teach that one or more of the binding species may bind to a particular

analyte that is in contact with the solid support having the array of species (col. 23, lines 64-67), and that multiple distinct analytes may be detected (see col. 24, lines 6-17).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize a solid support having an array of binding species as taught by Zarling et al. because Zarling et al. teach that such a solid support having an array of probes as an alternative embodiment wherein the solid support is a bead, such as the Velander et al. beads. Also, Zarling et al. teach that the solid support may have an array of different probes that bind to different analytes. One of ordinary skill in the art would recognize that the solid support having an array of probes provides the same function of immobilizing probes as beads, and that an array of different probes provides the benefit of detecting a plurality of analytes, as would be desirable for convenience.

Also, as to independent claim 1, although Velander et al. teach that because the protein 7D7 only binds protein C and prothrombin in the absence of metal ions, a buffer is used that contains a chelating agent, and gives an example of ehtylenediaminetetraacetic acid (EDTA) as a chelating agent, (see col. 13, lines 56-59), Velander et al. do not teach that the metal chelating agent may be a polysaccharide, such as apple pectin (as claimed in claims 1, 3-5 and 14-16). However, Kartel et al. teach the motivation to use a polysaccharide, such as apple pectin.

Kartel et al. teach that polysaccharides such as apple pectin is a metal chelator and it has a high selectivity for certain metals (see abstract and page 2592 and page 2595). While the Kartel et al. reference discloses use of apple pectin as a metal chelator for removal of metal ions from an organism (page 2596), Kartel et al. also disclose an *in*

vitro assay to evaluate the binding properties of apple pectin (see abstract and also page 2592). Kartel et al. found that apple pectin has high selectivity for certain metals (see abstract and page 2592 and 2595).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize apple pectin as the metal ion chelator generally disclosed by Kartel et al. as the specific metal ion chelator generally disclosed by Velander et al. because Kartel et al. teach that apple pectin provides the advantage of having high selectivity towards metal ions and is efficient in absorbing metal ions. That is, while Velander et al. teach the general use of a chelating agent (and discloses EDTA only as an example), Kartel et al. teach that the motivation for using apple pectin as the metal chelator by teaching that apple pectin is a metal chelator that has high affinity towards certain metal ions (see bottom of page 2595 for example). While the Kartel et al. reference does not disclose use of apple pectin in an assay other than the assay for the evaluation of the binding affinity of apple pectin, the reference nevertheless discloses that apple pectin acts as a metal ion chelator in an *in vitro assay*, and the Kartel et al. reference is analogous art because it relates to the same problem to be solved in the Velander et al. reference, i.e., metal chelating. Moreover, one of ordinary skill in the art would have reasonable expectation of success in utilizing apple pectin as the specific chelating agent generically disclosed by Velander et al. because Velander et al. do not limit the disclosed assay to any particular metal chelator but rather teach the use of a metal chelator in general (see col. 5, lines 17-20), and also because Kartel et al. teach that the apple pectin shows this high affinity for certain metal ions in an *in vitro* assay.

As to claim 10, Velander et al. disclose that the analyte is a protein (protein C, col. 13, line 56).

As to claim 12, Velander et al. disclose a plurality of washings steps between said contacting and detecting steps (col. 13, lines 63-64, and lines 67-68, and col. 1, lines 1-2).

6. Claims 13-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Velander et al., 5,328,603, in view of Zarling et al., 5,674,698, and further in view of Kartel et al., "Evaluation of Pectin Binding of Heavy Metal Ions in Aqueous Solutions", Chemosphere, Vol. 38, No. 11, pp. 2591-2596, 1999, Schoemaker et al., 4,837,167, and Pronovost et al., 5,773,234, and Wohlstadter et al., 6,207,369.

As to claims 13-16, Velander et al. in view of Zarling et al. and Kartel teach the invention substantially as claimed (see above under subheading 5), except for extracting the analyte from a cellular source in an extraction buffer and labeling the analyte in a buffer that is the same as the extraction buffer.

However, Schoemaker et al. teach that labeling an analyte prior to the step of contacting the analyte to the immobilized probed provides the advantage of eliminating a washing step and an improvement in kinetics of the reaction (see col. 2, lines 15-35). It would have been obvious to one of ordinary skill at the time the invention was made to label the analyte in the invention taught by Velander et al. in view of Zarling et al. and Kartel et al. as taught by Schoemaker et al. because Schoemaker et al. teach that this provides the advantages of eliminating a washing step and improving reaction kinetics.

Also, Velander et al. and Zarlng et al. and Kartel et al. do not teach employing the same buffer composition for the extraction and labeling step. However Pronovost et al. teach this limitation.

Pronovost et al. teach using a buffer in an extraction step, the buffer increasing the sensitivity of the assay, and preferably using the same buffer composition during labeling (col. 4, lines 48-61). It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the same buffer composition in the invention taught by Velander et al. in view of Zarling et al. and Kartel et al. because Pronovost et al. teach that using the same buffer, which increases sensitivity of the assay, in the labeling step is preferable. Given the teachings of Pronovost et al. of using the same buffer composition for the extraction step as the labeling step, one of ordinary skill in the art would have reasonable expectation of success in utilizing the same buffer for the extraction and labeling step in the invention taught by Velander et al. in view of Zarling et al. and Kartel et al.

Also, Velander et al. do not teach determining the presence of at least two distinct analytes in said sample.

However, Wohlstadter et al. teach that an array of immobilized probes may have different geometric shapes representing binding domains specific for different analytes (col. 8, lines 20-23). It would have been obvious to one of ordinary skill in the art at the time the invention was made to provide different probes in the array in the invention taught by Velander et al. (in view of Zarling et al., Kartel et al., Schoemaker et al., and Pronovost et al.) because Wohlstadter et al. teach that such an array of probes bind to

different analytes. One of ordinary skill in the art would recognize that the array provides the benefit of detecting more than one analyte.

As to claim 17, Velander et al. teach that the method is considered a method of determining a protein expression profile for the sample (col. 13, line 56).

Response to Arguments

Applicant's arguments with respect to the above rejected claims have been considered but are not persuasive.

Applicant argues that Examiner has provided no suggestion or motivation for replacing the metal chelating agent in the Margherita reference with the metal ion chelating polysaccharide of Kartel et al. Applicant argues that EDTA has substantial structural differences from the metal ion chelating polysaccharides of Kartel et al. as well as distinct metal ion binding characteristics and that given these facts, one of skill in the art would not be motivated to replace EDTA with the metal ion binding polysaccharides of Kartel et al. This is not persuasive because, as elaborated above, Kartel et al. teach that the motivation for using apple pectin as the metal chelator by teaching that apple pectin is a metal chelator provides the advantage of having high affinity towards certain metal ions (see bottom of page 2595 for example). As to Applicant's argument regarding the replacement of EDTA with apple pectin, this argument is not persuasive because Margherita teaches *in general* the use of a chelating agent for removal of metal ions and only lists EDTA as an example. Thus, it is

not necessary that the secondary reference teach a motivation for replacing EDTA specifically.

Applicant also argues that Kartel et al. is not analogous art to the field of Applicant's endeavor. Specifically, Kartel et al. is drawn to determining the applicability of certain manufactured pectins as food additives based on their metal binding properties, and that Kartel et al. is not drawn in any way to analyte detection assays as is claimed. This is not persuasive because the Kartel et al. references relates to the same problem to be solved in the Velander et al. reference, i.e., metal chelating, and therefore one of ordinary skill in the art would research that particular field and use teachings from Kartel et al. because it discloses metal chelators with high affinity for certain metal ions.

On page 9, Applicant also argues that unexpected results. Applicant submitted a declaration under 37 C.F.R. 1.132 in an attempt to show experiments that demonstrates an unexpected reduction in the background fluorescence in analyte binding assays that include metal ion chelating polysaccharides in the buffer over those that do not. Applicant states that this unexpected reduction in background fluorescence leads to increased sensitivity of the claimed analyte detection assays. Applicant argues that the prior art of record fails to teach that any metal ion chelating agent, let alone the polysaccharide metal ion chelating agents claimed, reduce background fluorescence to such an extent.

The Declaration under 37 CFR 1.132 filed September 29, 2006 is insufficient to overcome the rejection of any of the claims based upon prior art as set forth above for the following reasons.

The Declaration has not demonstrated unexpected results. Applicant's argument and the Declaration do not state what was expected and thus the results obtained by Applicant are unexpected. Merely because the use of a metal chelating polysaccharide showed a reduction in the background fluorescence does not show that this was unexpected. As disclosed by Kartel et al., apple pectin has high affinity towards certain metals. The primary references teach use of metal chelators for removing metal ions during an assay. There is no showing by Applicant that the reduction in the background fluorescence is not to be expected, especially given the disclosure of Kartel et al.

Moreover, while the Declaration states that the assays with and without metal chelating polysaccharide were performed under standard assay conditions, the Declaration does not state that *all* conditions of both the assays were the same (other than the difference in the metal ion chelator). If the conditions were different, this may affect the result and thus a proper comparison cannot be made.

Also, it is not clear in the Declaration whether or not the sample without the metal chelating polysaccharide included a non-polysaccharide metal chelator (such as EDTA). If the sample *without* the metal chelating polysaccharide did *not* have any metal ion chelator such as EDTA, then the difference in the background fluorescence may be due to the lack of *any* metal ion chelator as opposed to any differences between the metal

ion chelating polysaccharide and a non-polysaccharide metal ion chelator such as EDTA.

Also, the Declaration does not state that the metal chelating polysaccharide is specifically apple pectin, which is recited in claim 5, and thus it is not clear whether apple pectin or another metal chelating polysaccharide was used.

Also, while the Declaration states that Exhibit A shows the results of two assays and that the data in Exhibit A clearly demonstrate that the background fluorescence on the array contacted with the sample containing pectin is far lower than the background fluorescence on the array contacted with the sample without pectin, Exhibit A itself however does not show any data. It appears the data was blacked out.

For all of the above reasons, Applicant's Declaration is not sufficient to overcome the 103 rejections above.

Turning back to Applicant's arguments on page 12 in the response to the previous Office action, Applicant makes the same arguments for the rejections under Velander et al. as made for the rejections under Margherita. More specifically, Applicant's argue that merely citing another reference that teaches a buffer composition containing EDTA without addressing the deficiencies in providing a suggestion or motivation and a reasonable expectation of success fails to remedy the deficiencies in Examiner's prima facie case of obviousness. This is not persuasive because, as indicated earlier, Kartel et al. teach the motivation to utilize apple pectin by teaching that apple pectin provides the advantage of having high selectivity towards metal ions and is efficient in absorbing metal ions. Moreover, as indicated above, one of ordinary skill in

the art would have reasonable expectation of success in utilizing apple pectin as the specific chelating agent generically disclosed by the primary references (Margherita and Velander et al.) because the primary references do not limit the disclosed assay to any particular metal chelator but rather teach the use of a metal chelator in general (see Margherita, col. 13, lines 57-58, and see Velander et al., col. 5, lines 17-20), and also because Kartel et al. teach that the apple pectin shows this high affinity for certain metal ions in an *in vitro* assay.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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ANN YEN LAM
PATENT EXAMINER

12/4/06